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- Clin Pharmacol Ther. 2000 Jun;67(6):690.

Grapefruit juice greatly increases serum concentrations of lovastatin and lovastatin acid.

Kantola T, Kivisto KT, Neuvonen PJ.

Department of Clinical Pharmacology, University of Helsinki, Finland.

BACKGROUND: Grapefruit juice increases the bioavailability of several drugs known to be metabolized by CYP3A4. We wanted to investigate a possible interaction of grapefruit juice with lovastatin, a cholesterol-lowering agent that is partially metabolized by CY P3A4. METHODS: An open, randomized, two-phase crossover study with an interval of 2 weeks between the phases was carried out. Ten healthy volunteers took either 200 ml double-strength grapefruit juice or water orally three times a day for 2 days. On day 3, each subject ingested 80 mg lovastatin with either 200 ml grapefruit juice or water, and an additional dose of 200 ml was ingested 1/2 and 1 1/2 hours after lovastatin intake. Serum concentrations of lovastatin and lovastatin acid were measured up to 12 hours. RESULTS: Grapefruit juice greatly increased the serum concentrations of both lovastatin and lovastatin acid. The mean peak serum concentration (Cmax) of lovastatin was increased about 12-fold (range, 5.2-fold to 19.7-fold; $p < 0.001$) and the area under the concentration-time curve [AUC(0-12)] was increased 15-fold (range, 5.7-fold to 26.3-fold; $p < 0.001$) by grapefruit juice. The mean Cmax and AUC(0-12) of lovastatin acid were increased about fourfold (range, 1.8-fold to 11.5-fold; $p < 0.001$) and fivefold (range, 2.4-fold to 23.3-fold; $p < 0.001$) by grapefruit juice, respectively. The half-lives of lovastatin and lovastatin acid remained unchanged. CONCLUSIONS: Grapefruit juice can greatly increase serum concentrations of lovastatin and its active metabolite, lovastatin acid, probably by preventing CYP3A4-mediated first-pass metabolism in the small intestine. The concomitant use of grapefruit juice with lovastatin and simvastatin should be avoided, or the dose of these 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors should be reduced accordingly.

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☐ 1: J Clin Pharmacol. 1990 Dec;30(12):1128-35.

Related Articles, Links

Comparative pharmacokinetics and pharmacodynamics of pravastatin and lovastatin.

Pan HY, DeVault AR, Wang-Iverson D, Ivashkiv E, Swanson BN, Sugerman AA.

Squibb Institute for Medical Research, Princeton, NJ 08543-4000.

The oral bioavailability of two HMG-CoA reductase inhibitors, pravastatin and lovastatin, was investigated in this randomized, two-way crossover study. Twenty healthy men were randomly assigned to treatment with a 40-mg dose of pravastatin or lovastatin once daily for 1 week; steady state kinetics were assessed after the last dose. After 1 week of washout, each subject received the alternate treatment. Serum specimens were assayed by gas chromatography/mass spectrometry (GC/MS) for intact pravastatin or lovastatin acid and by bioassay for active inhibitor concentration and, after hydrolysis of lactones, for total inhibitor concentration. The systemic bioavailabilities of total (active plus potentially active) inhibitors for the two drugs were different, with the mean AUC value for lovastatin being 50% higher than that of pravastatin (mean +/- SEM AUC0-24 values of 285 +/- 25 and 189 +/- 13 ng-equiv x hr/mL, respectively, P less than .0001). Pravastatin, which is administered as the monosodium salt, is present in the systemic circulation as the open acid; lovastatin, which is administered as the lactone, is present as both open-acid active metabolites (62%) and closed-ring lactone metabolites (38%), which are potentially active. Based on mean AUC values, pravastatin accounted for 75% of the active inhibitors from a pravastatin dose. Lovastatin acid accounted for just 25% of the active inhibitors from a lovastatin dose, with the remainder due to other active metabolites. Significant decreases from baseline in total and low-density lipoprotein (LDL) cholesterol were observed during the first treatment leg for both pravastatin and lovastatin.(ABSTRACT TRUNCATED AT 250 WORDS)

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J Clin Pharmacol. 1990 Dec;30(12):1128-35.
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